EECS C145B / BioE C165: Image Processing and Reconstruction Tomography

Lecture 14

Jonathan S. Maltz

jon@eecs.berkeley.edu
http://muti.lbl.gov/145b
510-486-6744

Topics covered

1. Introduction
2. Basic nuclear magnetic resonance (NMR) physics
3. Relaxation processes
4. Instrumentation for NMR and magnetic resonance imaging
5. Pulse sequences and contrast determination
6. Physics of contrast
7. Tissue contrast in MRI
8. MR Frontiers: using paramagnetic tracers to image gene expression

Reading

Assigned reading:

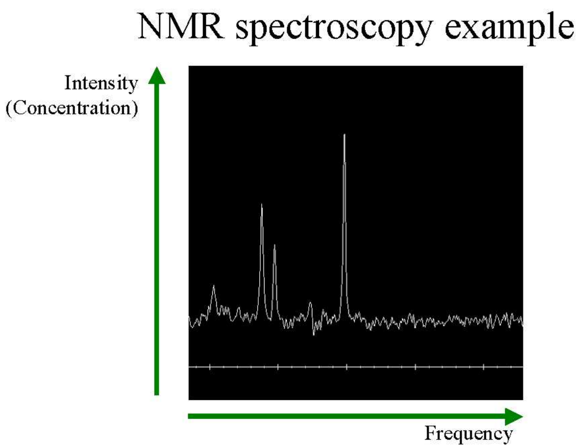
- MRI - The Basics pp. 16-66 (in course Reader)
- Course reader pp. 445-458
- MRI Primer pp. 41-195 (in course Reader)

Additional reading:

- Cho, "Foundations of Medical Imaging", John Wiley and Sons (1993), Chapters 9 and 10.
- Webb, "The Physics of Medical Imaging", Institute of Physics Publishing (1998), pp. 389-487.
- Oldendorf, "MRI Primer", Raven Press (1991).

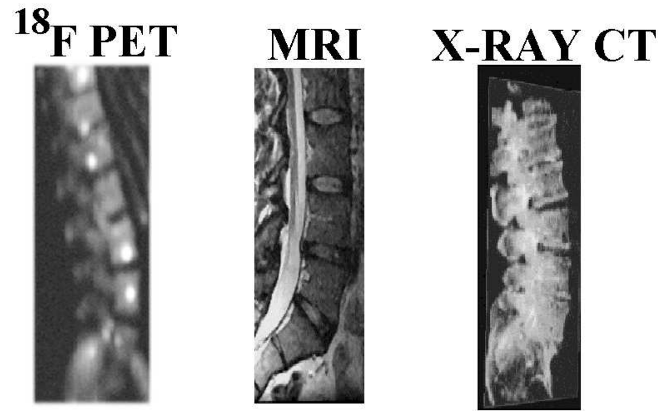
Introduction to NMR an MRI

- Nuclear magnetic resonance is a method of investigating **chemical composition**.
- It is based upon the **manipulation of nuclear spins** using magnetic fields.
- These fields are set up in space and time so that nuclei **resonate** or "sing" at **different frequencies** depending on the **molecular environment** that they find themselves.
- In **magnetic resonance imaging**, we investigate molecular environment as a **function of position in space**.
- Since different tissues and fluids flowing at different rates offer different molecular environments to nuclei, **contrast** can be obtained between these tissues or fluids.



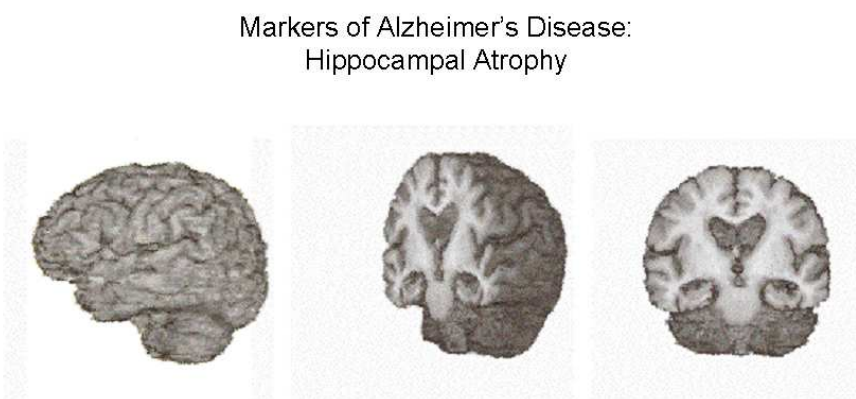
Source: Watts, Cornell

Different molecular species in a mixture appear as distinct peaks in the NMR spectrum. Each peak thus betrays the presence of a particular species. NMR spectroscopy is a powerful tool in analytical chemistry.



Source: DNMFI, LBNL

MR images exhibit strong contrast between soft tissue types. CT images tend to exhibit contrast between hard and soft tissues. MR and CT provide higher resolution images than PET. PET images function rather than anatomy (here, metabolism in bone is imaged).



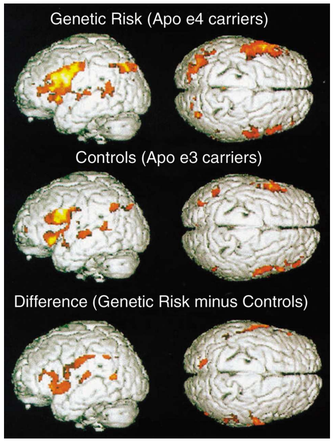
Source: DNMFI, LBNL

These 3D MR images of the brain show strong contrast between brain tissue and cerebrospinal fluid in the ventricles. Ventricular enlargement occurs in Alzheimer's disease and can be used to track its progression.

Source: Watts, Cornell

Injected magnetic contrast agents can be used in MRI. The circulatory system can be mapped in this way.

Introduction to NMR and MRI



In functional MRI (fMRI), contrast is based on blood oxygen level. Areas of the brain that are activated during cognition may be identified in real time. More hemoglobin is converted to deoxyhemoglobin in these areas. Here, the fMRI image is superimposed on an anatomical image. MRI has very high temporal resolution (source: Bookheimer et al. in Petrella et al., Radiology (2003)).

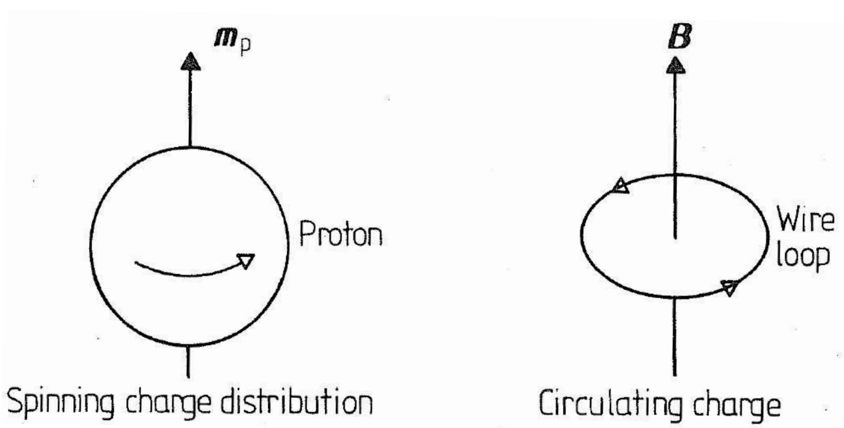
Basic physics: nuclear spin

- Felix Bloch at Stanford theorized that **spinning charged particles** create a **magnetic field.** He won the 1946 Nobel prize for this theory.
- Atomic nuclei **spin** and contain **positively charged** protons
- Nuclei have quantized **energy levels** related to their **spin quantum number** S:

$$N_e = 2S + 1$$

- In MRI, we are primarily concerned with the hydrogen $({}^1_1H)$ nucleus, which contains a single proton and for which $S = \frac{1}{2}$. Hydrogen gives a very strong MR signal as it is very abundant in living tissues. In which tissues is it highly abundant?

Basic physics: nuclear spin



Source: Webb p. 392

Basic physics: nuclear spin

- The proton has $N_e = 2\frac{1}{2} + 1 = 2$ energy states, denoted $-\frac{1}{2}$ and $\frac{1}{2}$.
- These states correspond to spins in opposite directions.
- The **right-hand rule** gives the direction of the field created by a spinning proton.
- In the absence of an applied magnetic field, the directions of the spins of protons in a quantity of matter are **random**. Statistically, an equal number of protons will have fields orientated in **anti-parallel** (anticlockwise spin) and **parallel** (clockwise spin) directions. Formally, the **magnetic dipole moment** (MDM) of a proton is proportional to its angular momentum:

$$\mathbf{m_p} = \gamma \mathbf{I}$$

where γ is the **gyromagnetic ratio**.

Basic physics: nuclear spin

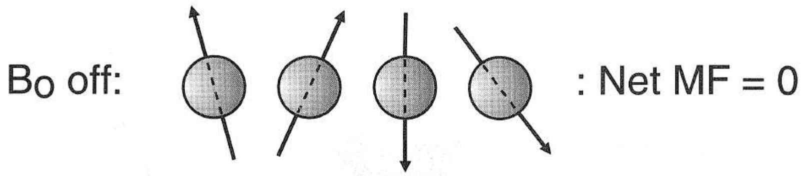


Figure 2-13. In the absence of an external magnetic field B_0, no net magnetization is produced by protons.

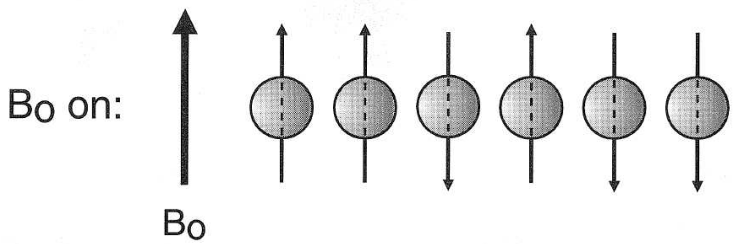


Figure 2-14. In the presence of an external magnetic field B_0, net magnetization is produced.

Source: Hashemi p. 24

Basic physics: nuclear spin

- For the classical model of the proton, which has charge $+e$ and mass m,

$$\gamma = \frac{e}{2m}$$

- γ has SI units of Hz/T.
- If we choose two protons with opposite spins, the **paired** fields cancel out leaving zero resultant magnetization in the nucleus.
- In nuclei with odd numbers of protons, a net magnetic field is produced, leading to a non-zero MDM.
- An externally applied magnetic flux density $\mathbf{B}_0$ exerts a torque or couple $\mathbf{C}$ on the MDM according to:

$$\mathbf{C} = \mathbf{m_p} \times \mathbf{B_0} = \frac{\mathbf{dI}}{\mathbf{dt}}$$

  where the second equality follows from Newton's Second Law. This is the classical model of spin as opposed to the quantum model.

Basic physics: nuclear spin

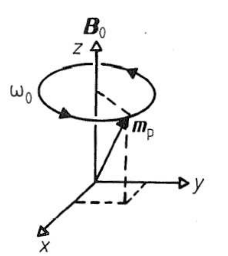


Figure 8.2 The interaction of a magnetic moment $\boldsymbol{m}_p$ with a magnetic flux density $\boldsymbol{B}_0$ results in the magnetic moment experiencing a couple $\boldsymbol{C}$ which produces motion (precession) with angular velocity ω_0 about $\boldsymbol{B}_0$.

Source: Webb p. 393

Basic physics: nuclear spin

- Substituting our previous expression for $\mathbf{I}$ yields the very famous and important **Larmor equation**,

$$\frac{d\mathbf{m_p}}{dt} = \gamma \mathbf{m_p} \times \mathbf{B_0}$$

  which describes the motion of the MDM about the applied field. This motion is called **precession**. Precession is periodic, and occurs at the frequency

$$\omega_0 = -\gamma \mathbf{B}_0$$

  ω_0 gives us the resonant frequency of a nucleus given an applied flux density B_0. We will see later how we can make a nucleus "sing" at this frequency.

- In MRI, we usually apply $\mathbf{B}_0$ in the z-direction along the axis of the patient so we can image transaxial slices.

Basic physics: nuclear spin

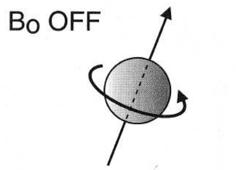


Figure 2-18. In the absence of an external magnetic field B_0, a proton rotating about its own axis generates a magnetic field.

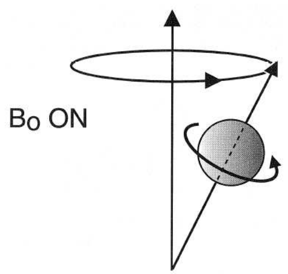


Figure 2-19. In the presence of an external magnetic field B_0, a proton not only rotates about its own axis but also "wobbles" about the axis of B_0.

Source: Hashemi p. 26

Basic physics: nuclear spin

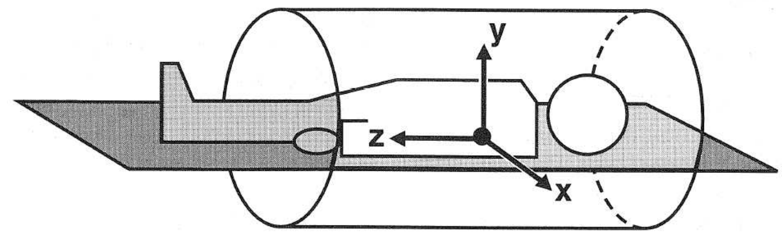


Figure 2-22. An arbitrary designation of x, y, and z for a patient in the scanner.

Source: Hashemi p. 26

Basic physics: nuclear spin

- If the MDM is parallel to B_z, then component of $\mathbf{m_p}$ in the x-y plane, m_{pxy} is zero and no torque acts on the MDM.
- When material containing many nuclei is subjected to $\mathbf{B}_0 = B_z$, the nuclei align with this field. The net magnetization of all nuclei $\mathbf{M} = M_z$ hence has no x-y component.
- In NMR, we take measurements of fields in the x-y plane.
- This means that we must apply another field parallel to this plane that **tilts the MDM away from the z-axis**.
- When we apply a field $\mathbf{B}_1$ oriented along the x-y plane that rotates at the Larmor frequency of the nucleus ω_0 (the same rate as $\mathbf{m_p}$), $\mathbf{M}$ experiences a second torque that tends to pull it away from the z-axis by an angle α.

Basic physics: nuclear spin

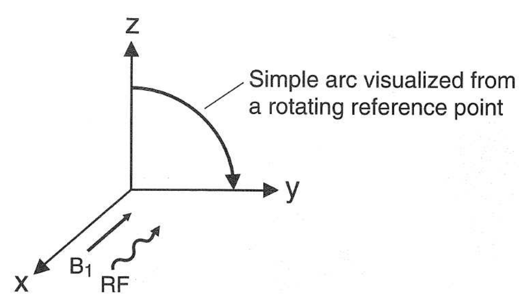


Figure 3-7. If the observer stands within the coordinate system, she would then see a simple arc motion rather than a spiral motion.

Source: Hashemi p. 36

Basic physics: nuclear spin

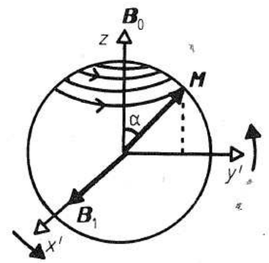


Figure 8.3 If a rotating magnetic flux density $\boldsymbol{B}_1$ is applied in the xy plane in the presence of a static field of flux density $\boldsymbol{B}_0$ orientated along the z axis, $\boldsymbol{M}$ will experience a torque $\boldsymbol{D}$ (in addition to the couple $\boldsymbol{C}$ which gives rise to precession about $\boldsymbol{B}_0$) moving $\boldsymbol{M}$ through an angle α from the z axis. (x' and y' are axes rotating at ω_0, the Larmor frequency (see §8.3.1.1).)

Source: Webb p. 393

Basic physics: nuclear spin

- The longer $\mathbf{B}_1$ is applied (τ_p), and the higher its magnitude, the closer $\mathbf{M}$ is pulled towards the x-y plane:

$$\alpha = \gamma_0 \int_0^{\tau_p} H_1(t)dt$$

- The rotating flux density $\mathbf{B}_1$ is produced by a circularly polarized applied **radio frequency** (RF) pulse at the Larmor frequency. The pulse is usually in the MHz range. The matching of the frequency of the RF pulse and the Larmor frequency is essential if **resonance** is to be achieved. Only then can $\mathbf{M}$ be pulled away from the z-axis.

Basic physics: nuclear spin

- The effect on the bulk magnetization $\mathbf{M}$ of an arbitrary applied field is governed by the same equation as that describing the effect of such a field on a single proton:

$$\frac{d\mathbf{M}}{dt} = \gamma \mathbf{M} \times \mathbf{B}$$

This is the most famous of the **Bloch equations**.

Basic physics: Bloch equations and relaxation times: T_1

- A very important RF pulse in NMR is designed to have the exact duration and power necessary to ensure that $\mathbf{M}$ is deflected by $\alpha = 90$ degrees, giving $M = M_{xy}$. This is called a 90 degree pulse.
- After the pulse is over, the spins of the nuclei interact with fields in the surrounding atomic lattice. Energy is transferred to and from the spinning nuclei via this interaction. These fields affect the rate at which the static applied field $B_z = B_0$ pulls $\mathbf{M}$ back to the z-axis. Another Bloch equation describes this process of **longitudinal relaxation**:

$$\frac{dM_z}{dt} = \frac{M_0 - M_z}{T_1}$$

where T_1 is the longitudinal or **spin-lattice** relaxation time and M_0 is the magnitude of $\mathbf{M}$ before the pulse was applied (when $\mathbf{M}$ was aligned with the z-axis).

Basic physics: Bloch equations and relaxation times

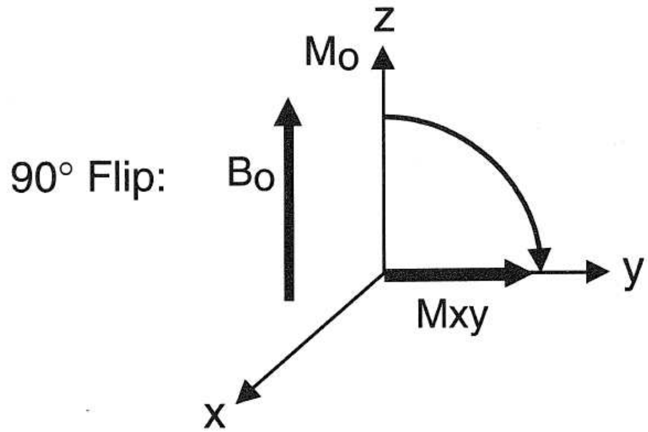
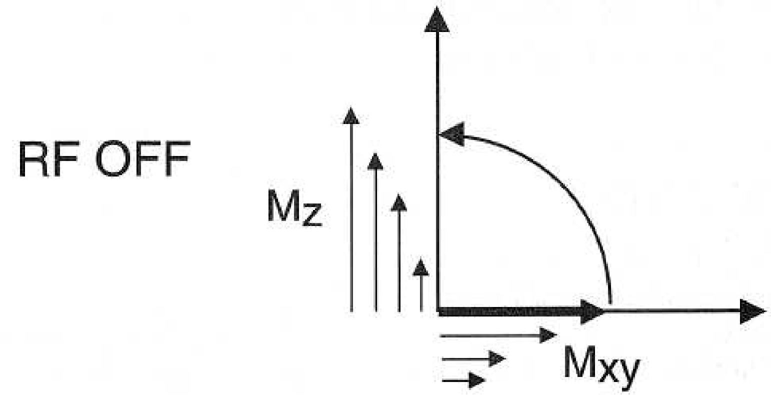


Figure 3-8. When the entire magnetization vector is flipped into the x-y plane, it is called a 90° flip.

Source: Hashemi p. 37

Basic physics: Bloch equations and relaxation times



Source: Hashemi p. 42

After the RF pulse ends, relaxation processes return **M** towards the z-axis so that it is again aligned with $\mathbf{B}_0$.

Basic physics: Bloch equations and relaxation times: T_1

- Longitudinal relaxation describes the process of the **recovery of the magnetization in the z-direction**.
- Immediately after a 90 degree pulse $M_z = 0$. Once equilibrium is reestablished, $M_z = M_0$. Solving the Bloch equation for the 90 degree flip gives:

$$M_z(t) = M_0\,(1 - \mathrm{e}^{-t/T_1})$$

- We see that T_1 is the time constant of the relaxation process that returns **M** to equilibrium under the influence of $\mathbf{B}_0$.
- This time constant is dependent on the atomic lattice surrounding the spinning nuclei. Thus, spatial differences in T_1 are related to the **properties of the material** in which the nuclei exist. Contrast in NMR can therefore be obtained that is based on differences in **chemical composition**.

Basic physics: Bloch equations and relaxation times: T_1

- Specifically, T_1 provides information relating to **vibration within the lattice or molecular environment.** In living organisms, **water molecules dominate** the spin-lattice relaxation interactions. T_1 is consequently a measure of the freedom of water molecules to tumble and rotate. This property is **tissue dependent**, as water is bound and absorbed differently in different tissue types.
- In CT, contrast is based on differences in electron density. NMR contrast can be **far more subtle and sensitive** and is based on small differences in the **molecular milieu** in which a nucleus finds itself.

Basic physics: Bloch equations and relaxation times: T_2

- A second type of relaxation occurs in which loss of magnetization in the x-y plane occurs. This is called **transverse relaxation**.
- Clearly, longitudinal relaxation reduces M_{xy}, but other processes work simultaneously to diminish M_{xy}.
- These processes induce **spin-spin** relaxation, which is due to the **loss in coherence** of spins caused by the interaction between the spins of nuclei in a neighborhood. This type of relaxation occurs by three different regimes.
- In a lattice, nearby nuclei will have spins that induce a small magnetization that has a component along the z-axis.
- These fields **modulate $\mathbf{B}_0$** so that different nuclei experience **slightly different longitudinal fields**. The frequency of precession is in turn modulated.

Basic physics: Bloch equations and relaxation times

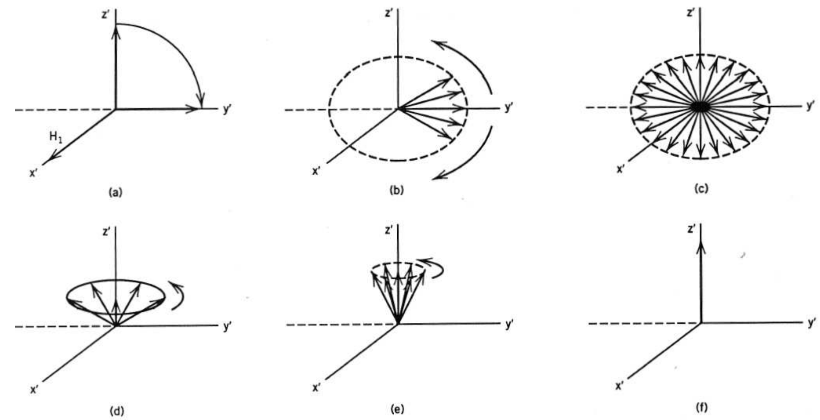


Figure 9-6 Sequential behavior of the spin relaxation processes. (a) The spin magnetization is flipped by an rf pulse $\mathbf{H}_1$. (b) The spins undergo dephasing due to the spin-spin relaxation and field inhomogeneity. (c) When fully dephased the FID signal decays to zero as the spins lose phase coherency. (d), (e), and (f) represent T_1 spins relaxation processes which lead to the recovery of the spins to the original equilibrium state via the spin-lattice relaxation process.

Source: Cho p. 248

Basic physics: Bloch equations and relaxation times: T_2

- Just after the application of the RF pulse, all spins are phase-synchronized in the x-y plane. As time elapses, slight differences in frequency **dephase** the individual $\mathbf{m_p}$'s resulting eventually in complete phase incoherence and canceling of $\mathbf{M}_{xy}$.
- The third Bloch equation describes this process as:

$$\begin{aligned} \frac{dM_x}{dt} &= -\frac{M_x}{T_2} \\ \frac{dM_y}{dt} &= -\frac{M_y}{T_2} \end{aligned}$$

Basic physics: Bloch equations and relaxation times: T_2

- After a 90 degree RF pulse, we have magnetization components along the x and y axes equal to M_x and M_y, respectively. At $t = \infty$, $M_x = M_y = 0$. T_2 relaxation for the 90 degree flip is thus given by:

$$\begin{aligned} M_x(t) &= M_x(0)\,\mathrm{e}^{-t/T_2} \\ M_y(t) &= M_y(0)\,\mathrm{e}^{-t/T_2} \end{aligned}$$

or

$$M_{xy}(t) = M_0\,\mathrm{e}^{-t/T_2}$$

- Usually, T_2 is much smaller than T_1.

Basic physics: Bloch equations and relaxation times: T_2

- A second process that leads to phase incoherence is the **exchange of spin states between two nuclei**. Energy is conserved within each spin system, but **phase information is lost.**
- The third regime by which phase coherence is lost is similar to the first, except that the variation in $\mathbf{B}_0$ is due to **inhomogeneities in the applied field**. Real world magnets do not have uniform fields and this leads to differential **spreading** of precession frequencies as a function of the **location of nuclei in the field.**

Basic physics: Bloch equations and relaxation times: T_2^*

- The effect of magnetic field inhomogeneities is **undesirable** and leads to errors in measured values of T_2. We separate this contribution and define the measured apparent T_2 as:

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \gamma \Delta B_0/2$$

  where ΔB_0 is the local inhomogeneity.

Quantum model of proton NMR

- The consequences of the application of a 90 degree pulse are easily understood in terms of the **classical theory** of nuclear spin.
- The other important pulse in NMR is the **180 degree pulse**. This pulse is best understood in terms of the quantum theory of NMR.
- We briefly review this theory, considering only the **single proton**.
- Consider a nucleus with spin angular momentum $\mathbf{I}$. Then:

$$\mathbf{I} = \hbar\sqrt{I(I+1)}$$

  where I is the nuclear spin quantum number $\left(\frac{1}{2} \text{ for the proton}\right)$, $\hbar = h/2\pi$ and h is Plank's constant.
- The uncertainty principal tells us that we cannot find the direction of $\mathbf{I}$. However, when we apply an external flux density $\mathbf{B}_0$, $\mathbf{I}$ is **quantized** and can therefore assume only a **limited number of values**. Energy levels are set up.

Quantum model of proton NMR

- When $\mathbf{B}_0$ is applied, the z component of $\mathbf{I}$ will be $m_I\hbar$, where m_I is the **magnetic quantum number** assuming the values of $\pm\frac{1}{2}$ for the proton.
- The proton thus has **two possible energy states**.
- We can relate these states to the classical theory.
- Protons with $\mathbf{m_p}$ **parallel** to $\mathbf{B}_0$ are in the **low energy state**.
- Protons with $\mathbf{m_p}$ **antiparallel** to $\mathbf{B}_0$ are in the **high energy state**.
- The energy of these states is:

$$E = -\gamma\hbar\, m_I B_0$$

- $\gamma\hbar$ is known as a **nuclear magneton**.

Quantum model of proton NMR

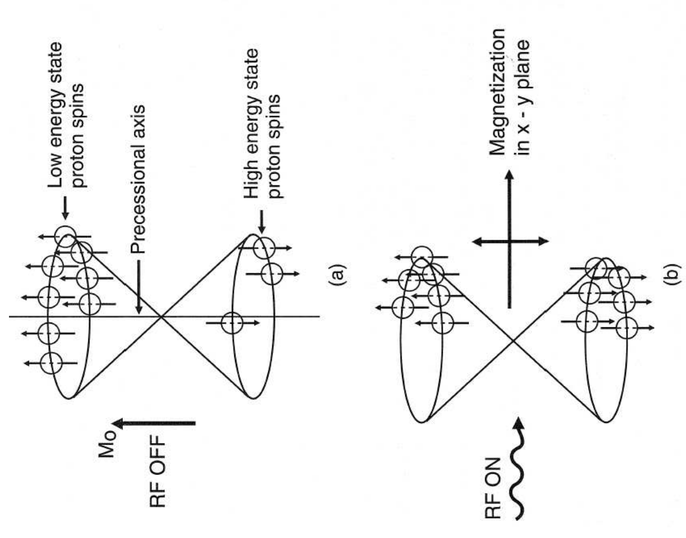


Figure 3-10. The application of the RF pulse (b) can equalize the number of north- and south-pointing protons.

Source: Hashemi p. 38

Quantum model of proton NMR

- A proton in the low energy state can be promoted to the high energy state by acquiring an energy:

$$\Delta E = E_2 - E_1 = -\gamma\hbar\Big[-\frac{1}{2} - \frac{1}{2}\Big]B_0 = \gamma\hbar B_0$$

- The frequency of the RF radiation that imparts this quantum of energy is given by:

$$\hbar\,\omega_0 = \gamma B_0\,\hbar$$

- This means that only an RF pulse at the **Larmor frequency** can promote a proton to the high energy state.

Quantum model of proton NMR

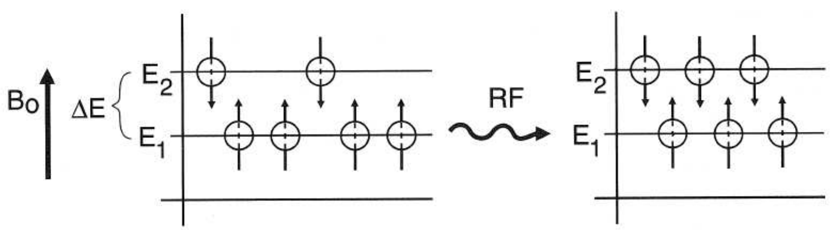


Figure 3-9. When placed in a magnetic field B_0, protons will fall into one of two energy states: in the lower energy state, protons are lined parallel to B_0, whereas in the higher energy state they are antiparallel to it.

Source: Hashemi p. 37

Quantum model of proton NMR

- The proton NMR signal is based on the **population difference** between the two energy states.
- Of the order of **one in a million** protons populates the high energy state (3×10^{-6} at 1T at room temperature).
- The NMR signal is thus very small. **RF pulse sequences** must be designed to achieve an acceptable SNR.
- The **180 degree pulse** plays an important role in many pulse sequences. It performs a **population inversion**.
- A population inversion **exchanges the energy states** of protons so that most populate the higher energy level.

Instrumentation: Basic system configuration

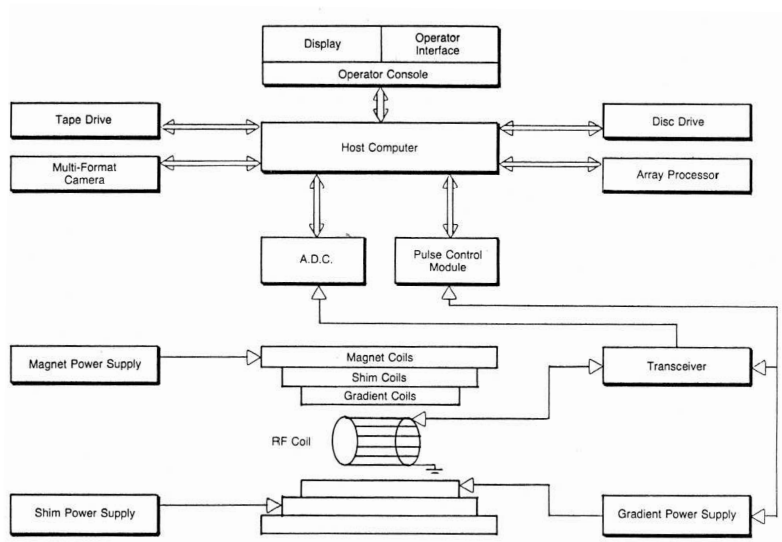


Figure 1.24 ▪ Block diagram of a typical MRI system.

Source: Shaw p. 39

Instrumentation: Basic system configuration

- The **main field** B_0 is almost always provided by a **superconducting magnet**. This magnet typically produces a flux density of $0.5 - 4$T for human MRI (most magnets in clinical use are 1.5T).
- **Shim coils** are used to **calibrate** the main field to make it as homogeneous as possible.
- **Gradient coils** produce magnetic fields that vary **linearly** in the x and y directions. These are used for **spatial encoding**, in other words, to make nuclei at **different positions resonate at different frequencies**. These fields are essential for image formation.
- An **RF coil** to induce the field $\mathbf{B}_1$ and listen to **free induction decay (FID)** signal proportional to the $\mathbf{m_{pxy}}$ of the nuclei.
- A **transceiver** that applies pulses to the RF coil and amplifies the incoming FID.
- **The output of an NMR system is the FID**.

The free induction decay

- After a 90 degree RF pulse is applied (inducing a field $\mathbf{B}_1$), the magnetization vector $\mathbf{M}$ lies in the x-y plane.
- As long as the spins remain in phase, the nuclei will produce an RF signal at their Larmor frequency ω_0. This signal is termed the **free induction decay**.
- The same coil that was used to **radiate** the pulse is therefore suitably tuned to **receive** the FID.
- Because of spin-spin relaxation, the spins do not remain in phase, and the FID is thus the **product of a sinusoidal carrier and a decaying real exponential**:

$$s(t) = S\cos(\omega_0 t + \phi)\,\mathrm{e}^{-t/T_2^*}$$

where S is a constant proportional to the number of nuclei contributing to the signal and ϕ is some phase constant.

The free induction decay

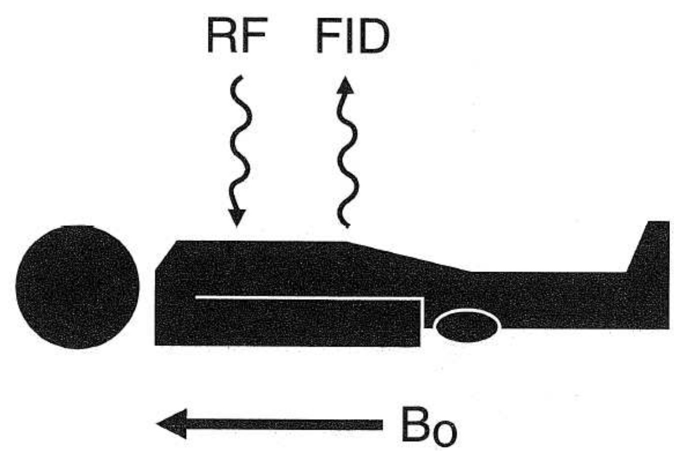


Figure 5-4. Immediately after transmission of the RF pulse, an FID is formed.

Source: Shaw p. 50

The free induction decay: no spin-spin interaction

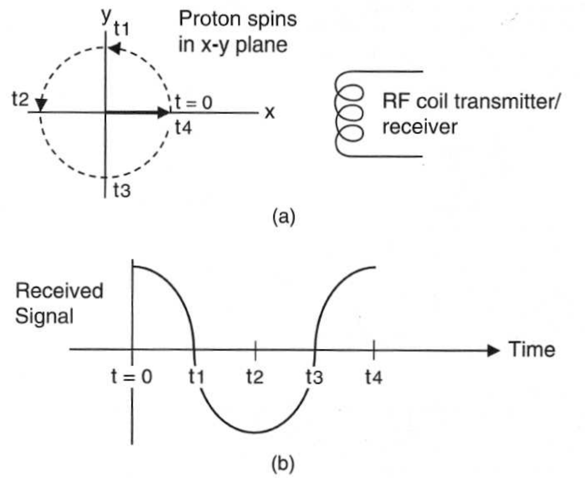


Figure 4-10. The relationship between transverse magnetization **(a)** and the received signal **(b)** at different points in time.

Source: Hashemi p. 46

The free induction decay: with spin-spin interaction

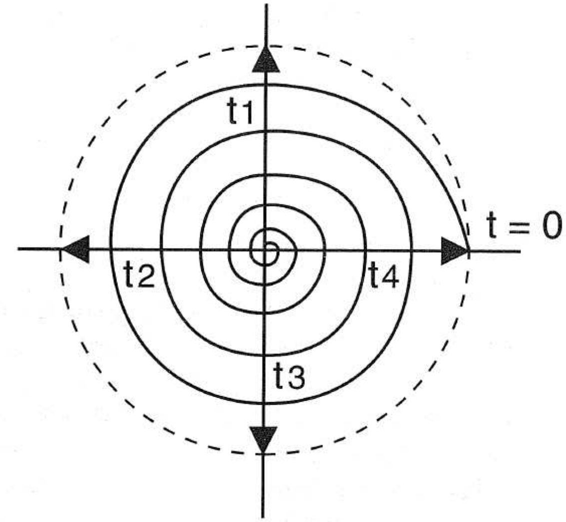


Figure 4-11. The spiral-like decay of transverse magnetization.

Source: Hashemi p. 47

The free induction decay: with spin-spin interaction

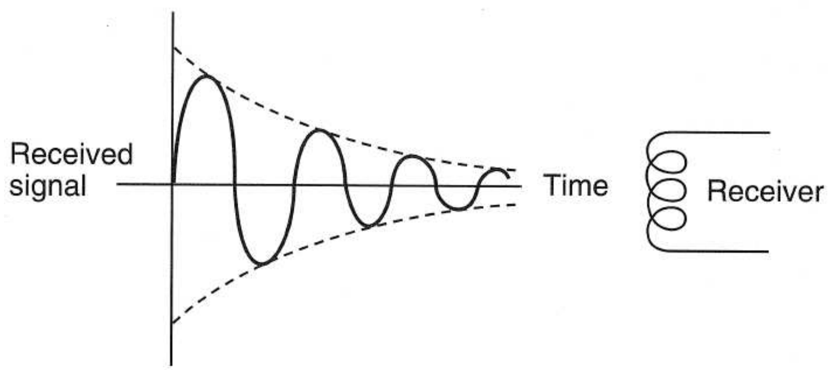


Figure 4-12. The decaying sinusoidal waveform of the received signal (the FID).

Source: Hashemi p. 47

The free induction decay: with spin-spin interaction

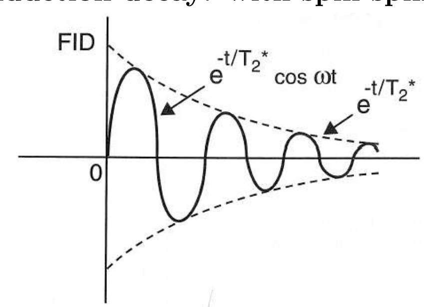


Figure 5-2. The received signal (the FID) has a decaying sinusoidal waveform.

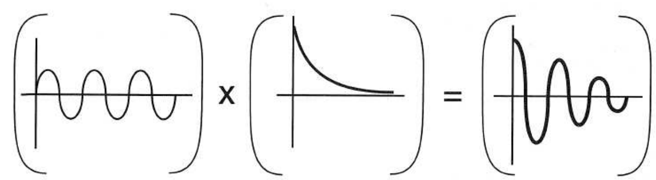


Figure 5-3. The product of a sinusoidal signal and an exponentially decaying signal results in a decaying sinusoidal signal.

Source: Hashemi p. 50

Spin echo

- Spin-spin interactions and field homogeneities **rapidly attenuate the FID** produced by a 90 degree pulse.
- If we **reverse the directions** of the spins (by performing a **population inversion**), we can **undo the effect** of T_2^* decay this is due to inhomogeneities in the **external field**, but not due to spin-spin interaction (the latter is not time-reversible).
- As a consequence, the FID will initially decay, but then start to grow again after the 180 degree pulse is applied.
- The FID will then decay a **second time.**
- The reemergence and decay of an FID is called a **spin echo**.
- Sequences that use spin echo techniques can double the SNR and remove the effects of field homogeneities.
- The time between the start of the original FID and its echo, the **echo delay time**, is denoted TE.
- The time between the 90 degree pulse and the 180 degree pulse is thus $TE/2$.

Spin echo

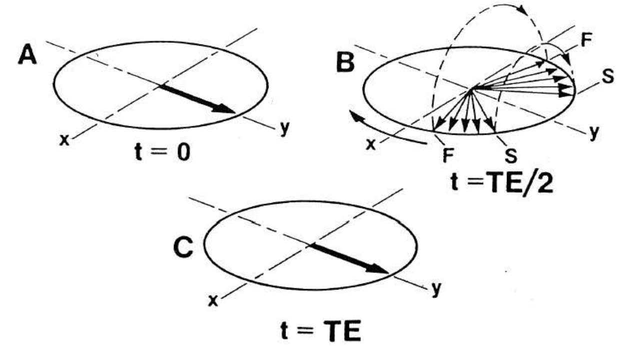


Figure 1.8 ▪ Spin-echo formation. Following a 90° pulse, the magnetization is along the y' axis (A). In an inhomogeneous magnetic field, some isochromats will be in a higher field than the mean and will precess faster than the mean (F), some nuclei will precess slower (S) (B). A 180° pulse applied $TE/2$ sec later along the y' axis rotates the nuclei as shown. A further $TE/2$ sec later, the fast isochromats will have caught up the slow ones and a spin echo is formed.

Source: Shaw p. 10

Isochromats are small neighborhoods each exposed to a homogeneous field.

Spin echo

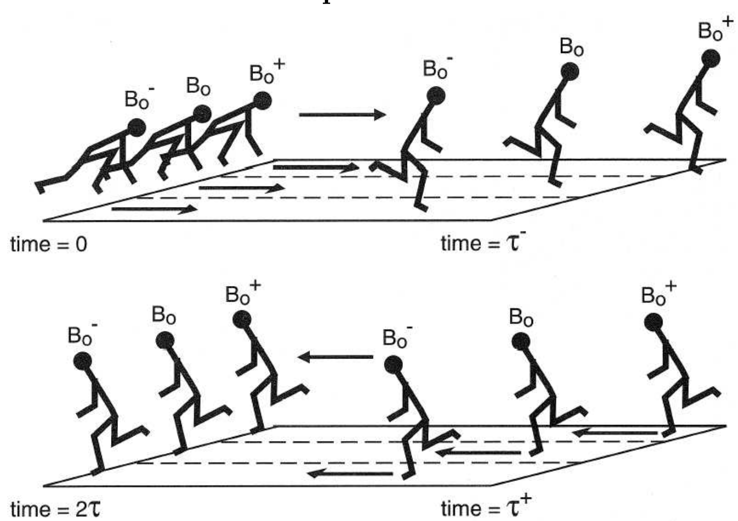


Figure 8-2. Analogy of three runners on a track. At time τ they are made to turn around and run back towards the starting point. Because the slowest runner is now in the lead, they will all reach the starting point at exactly the same time (at time 2τ).

Source: Hashemi p. 78

Spin echo

- By the time the FID at TE is sampled, it has decayed by e^{-TE/T_2}, but the effects of field inhomogeneities have been removed.
- MR images acquired with pulse sequences having **short** TE provide little contrast between tissue characterize by different T_2 values.
- These images are referred to as having **low T_2 weighting.**
- When TE is **long**, high contrast is achieved between tissues with differing T_2. These are referred to as **T_2-weighted images**.

Spin echo

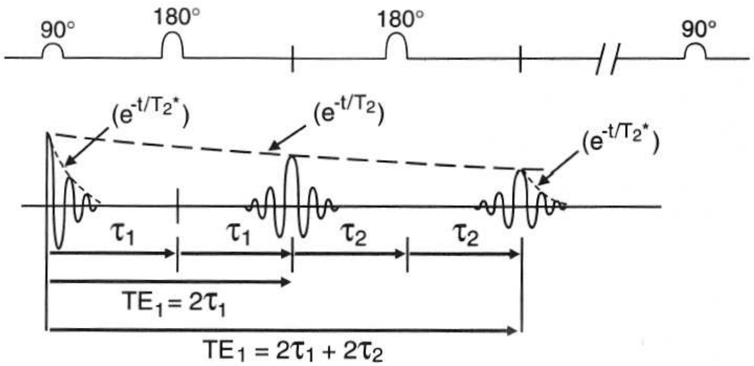


Figure 8-5. An example of a dual echo, spin echo pulse sequence in which two echoes are formed via application of two 180° pulses.

Source: Hashemi p. 80

Spin echo

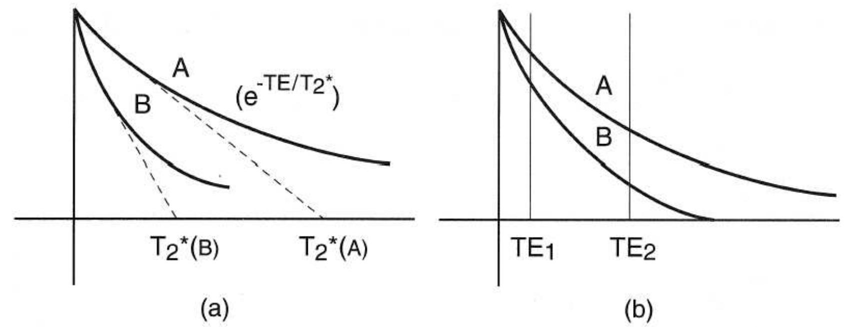


Figure 5-11. **(a)** Two tissues A and B with different T2*s. Which tissue has the longer T2? **(b)** Consider two different TEs on a decay curve. Which TE provides better tissue contrast between A and B?

Source: Hashemi p. 55

90 degree pulse repetition

- The time constant T_2^* describes the decay of the **envelope of the FID.** However, the starting value of the initial FID is governed by the recovery of M_z via spin-lattice relaxation (T_1).
- The recovery of M_z can be interrogated using repeated 90 degree pulses.
- The initial (peak) value of the FID following the first 90 degree pulse is $kM_z(t=0) = kM_0$, where k is a constant. This is because all the magnetization is flipped onto the x-y plane (after the pulse $M_{xy} = M_z(t=0) = M_0$).
- If, after a time TR, we apply another 90 degree pulse, the magnetization M_z will have recovered to:

$$M_z(TR) = M_0\left(1 - \mathrm{e}^{-TR/T_1})\right)$$

and so the peak of the FID will be only $kM_z(TR)$.

90 degree pulse repetition

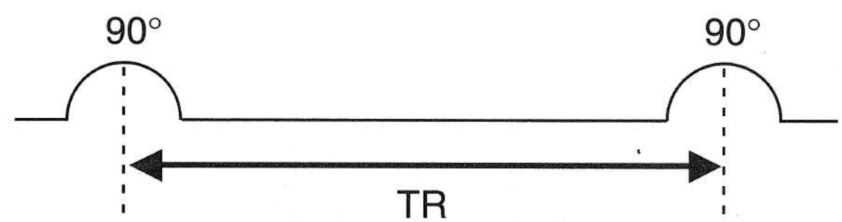


Figure 5-5. The time interval between two successive 90° RF pulses is denoted TR.

Source: Hashemi p. 51

90 degree pulse repetition

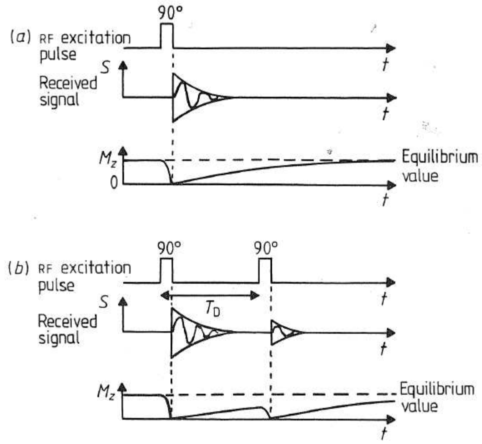


Figure 8.13 (*a*) The M_z component of magnetisation recovers to its equilibrium value following an initial 90° RF pulse of a saturation-recovery sequence; (*b*) the magnetisation M_z at time T_D can be monitored with a second 90° RF pulse in a saturation-recovery sequence.

Source: Webb p. 403

90 degree pulse repetition

- At later multiples of T_R, we will still have

$$M_z(nTR) = M_0\Big(1 - \mathrm{e}^{-TR/T_1}\Big), \qquad n \in \mathcal{Z}, n > 0$$

  because M_z will always recover to the same value during the time TR.

- To enhance T_1 contrast, we need to maximize the difference in the signals originating from tissues exhibiting different T_1 values.

- Because the slope of the curve:

$$M_z(t) = M_0\Big(1 - \mathrm{e}^{-t/T_1}\Big)$$

  is **steepest for small** t, T_1-weighted images are acquired using **short** TR pulse sequences.

90 degree pulse repetition

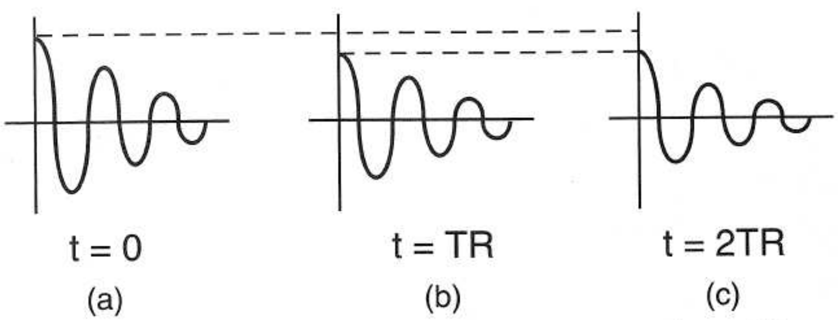


Figure 5-7. The FIDs after successive RF pulses: (a) at t = 0; (b) at t = TR; (c) at t = 2TR.

Source: Hashemi p. 52

90 degree pulse repetition

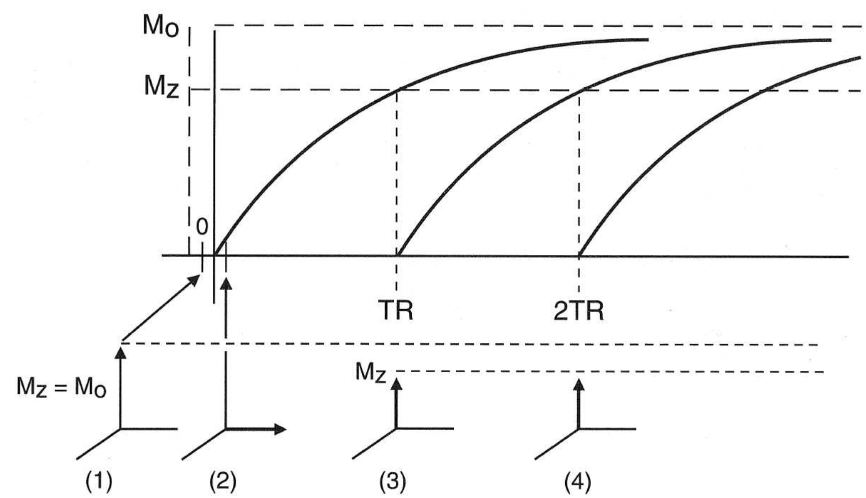


Figure 5-6. The recovery curves after successive RF pulses.

Source: Hashemi p. 51

90 degree pulse repetition

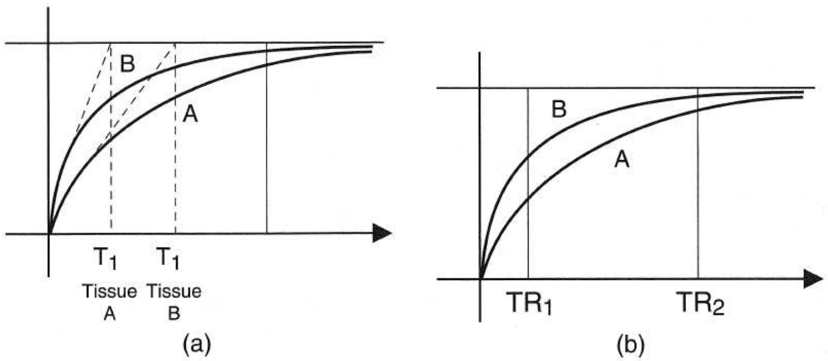


Figure 5-10. **(a)** Two tissues A and B with different T1s. Which tissue has the longer T1? **(b)** Consider two different TRs on a recovery curve. Which TR provides better tissue contrast between A and B?

Source: Hashemi p. 54

Spin density weighting

- The peak amplitude of the FID for a specific TR and TE is proportional to:

$$S \propto M_0\Big(1 - \mathrm{e}^{-T_R/T_1}\Big)\Big(\mathrm{e}^{-T_E/T_2}\Big)$$

- Now the local M_0 is proportional to the number of mobile protons $N(H)$, so:

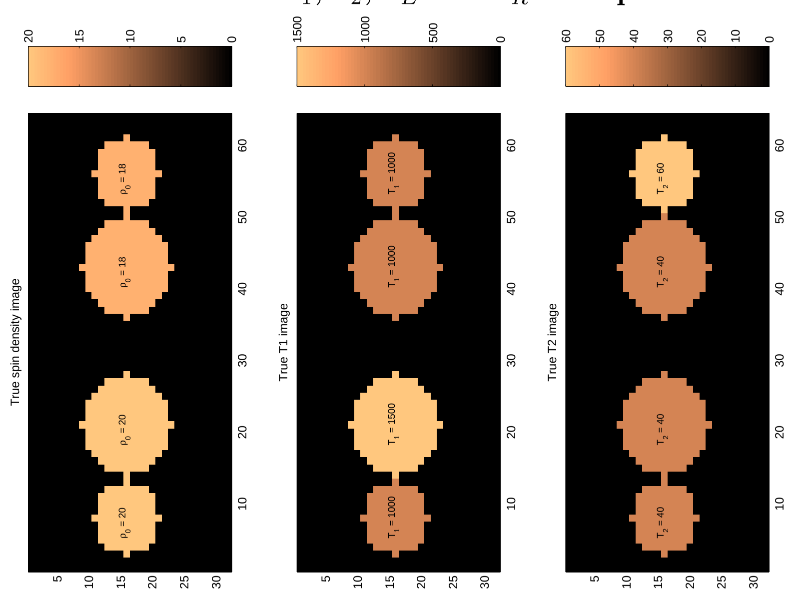
$$S \propto N(H)\Big(1 - \mathrm{e}^{-T_R/T_1}\Big)\Big(\mathrm{e}^{-T_E/T_2}\Big)$$

- If we make T_R long, we diminish T_1 contrast.
- If we also make T_E short and diminish T_2 contrast. In the limit:

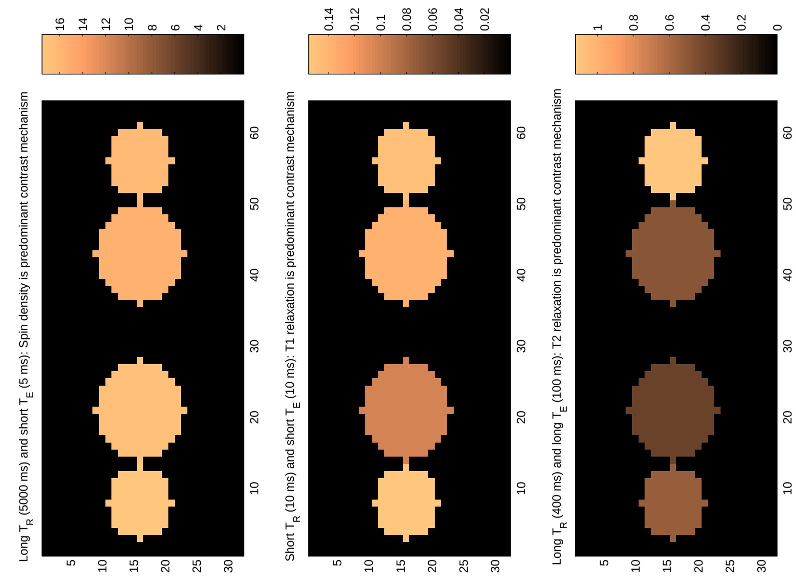
$$S \propto N(H)\Big(1 - 0\Big)\Big(1\Big) = N(H)$$

- Images acquired with such sequences are termed **spin density-weighted** or **proton density-weighted** images.

Contrast: T_1, T_2, T_E and T_R example



Contrast: T_1, T_2, T_E and T_R example



Tissue contrast: T_2

What properties of matter and living tissues influence T_2?

- The T_2 property of a tissue is determined by the **speed at which proton spins dephase.**
- In a tissue having a low T_2, spins dephase very fast.
- In fluids, molecules are always moving and interacting. This process is called **Brownian motion** and the frequency of interactions is determined by temperature and the viscosity of the fluid.
- The output of a Brownian motion process can be modeled as **broadband noise** extending from 0 Hz (DC) up to many GHz.

MRI contrast: Thermal noise (Brownian motion)

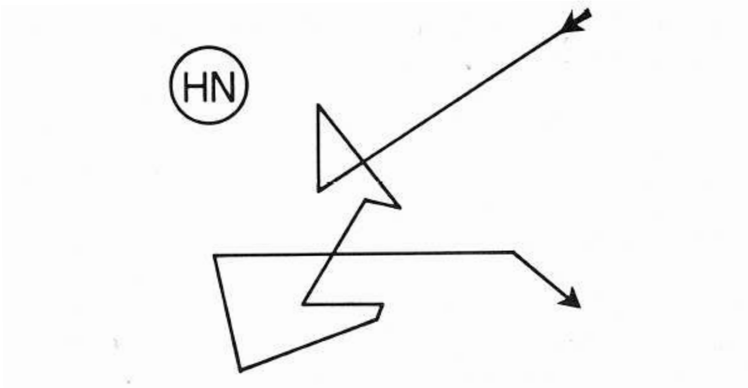


FIG. 5–3. In the liquid state a water molecule moves rapidly, changing direction and rotating as it undergoes many collisions and near collisions.

Source: Oldendorf p. 49

HN ≡ hydrogen nucleus

Tissue contrast: T_2

- Each molecular collision or "near miss" leads to a perturbation in the local magnetic field and contributes towards dephasing.
- **Thermal noise** thus adds to the external magnetic field to produce a local magnetic field that is noisy.
- Spin-spin relaxation is sensitive to thermal noise **regardless of its frequency.**

MRI contrast: Thermal noise (Brownian motion)

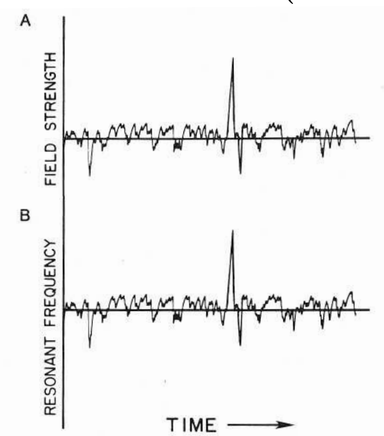


FIG. 5–4. A. Random fluctuations in field strength at a particular nucleus, due to the thermal motion of magnetic nuclei and atoms. In this imaginary graph, the large spike represents a very near miss with a strongly magnetic atom. **B.** The resonant frequency of the nucleus varies, precisely following changes in field strength. The random change in resonant frequency of each nucleus causes the degradation of phase relationship between nuclei, thereby determining T_2.

Source: Oldendorf p. 51

Tissue contrast: T_2

- If we raise the temperature of water being examined using NMR, what happens to T_2?

- T_2 is **long** ($\approx 2.5s$) in water because:
  1. The hydrogen atoms in a single molecule are separated from each other by an oxygen atom, and hence are **situated far apart**. This lowers internal spin-spin interaction.
  2. The distance between molecules in water is large. This **decreases the number of interactions** between molecules and hence the **power of the magnetic field thermal noise process.**
- T_2 is **short** in solids because atoms are closely packed into a lattice and protons are close enough to interact.
- T_2 is of **intermediate length** in fats and proteinaceous material because atoms are more closely spaced than in water, but less compactly arranged than in solids.

Tissue contrast: T_2 of tissues

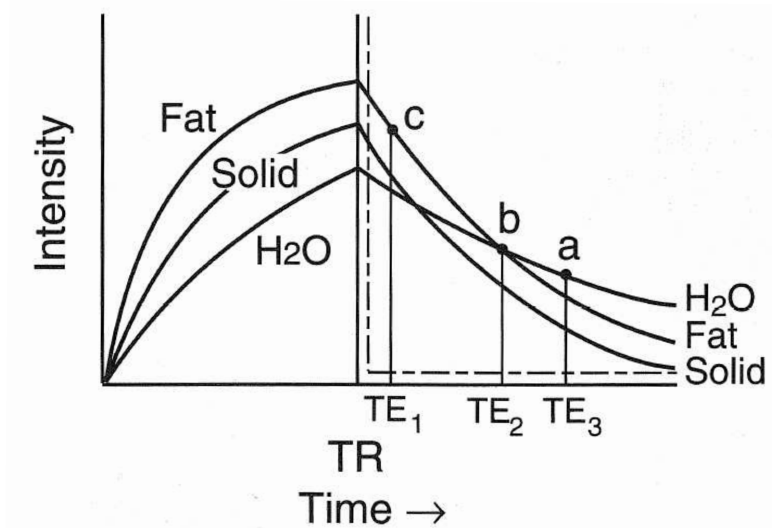


Figure 6-3. T2 decay curves of fat, water, and a solid tissue.

Source: Hashemi p. 60

Tissue contrast: T_1

What properties of matter and living tissues influence T_1?

- T_1 is the time constant describing the process whereby a nuclei **lose energy** imparted by the 90 degree RF pulse and return to equilibrium.
- Since Brownian motion is broadband noise, **some** of this thermal motion will induce noise in the local magnetic field **at the Larmor frequency.**
- The resonant system is sensitive to **any signal at this frequency** and so the rate of return to equilibrium will be affected.
- These fluctuations always serve to **reduce the energy of the spin system** and thus decrease T_1.
- Most thermal noise occurs above typical proton Larmor frequencies ($\omega_0 = 42.6 \times 10^6$ Hz/T) at room temperature.

Tissue contrast: T_1

- If we cool a sample of water (ensuring it remains liquid), will T_1 increase or decrease?

- The higher the temperature, the greater the spectral bandwidth. The further the noise is spread out in frequency, the lower its power over the band.
- In **water** at room temperature, the spectral bandwidth of the thermal noise is much **wider** than ω_0. The power of the spectrum in the NMR band is thus much lower. T_1 is **long** (≈ 2.5 s $\approx T_2$).
- In **solids**, the spectral bandwidth of the thermal noise is **somewhat lower** than ω_0. The NMR band falls in the "roll-off" region of the noise spectrum and more power consequently exists in the NMR band than was the case for water. T_1 is of **intermediate length**.
- In **fat and proteinaceous fluids**, spectral power is very high in the NMR band (near ω_0). T_1 is **short**. ω_0 and the peak of the spectrum almost coincide.

MRI contrast: Thermal noise (Brownian motion)

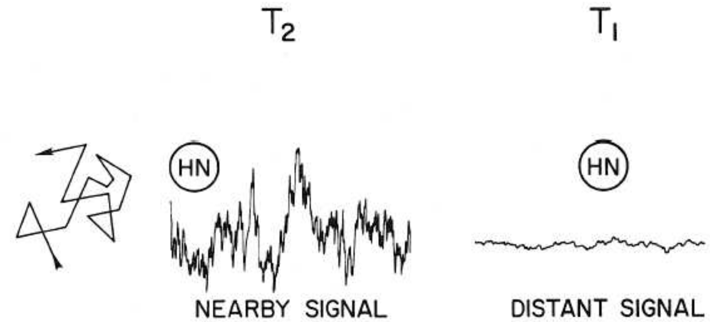


FIG. 5–8. The thermal motion of a magnetic nucleus causes strong random fluctuations in field strength at a nearby hydrogen nucleus (HN), whose Larmor frequency changes proportionately. Because the Larmor frequency of each of the nuclei in a region changes randomly, they become dephased, at a rate described as T_2. At a distant nucleus, such thermal motion produces weak perturbations that have little effect on the Larmor frequency. Perturbations from trillions of other distant sources combine to create a high-frequency magnetic signal containing some component at the resonant larmor frequency, thus triggering T_1 decay.

Source: Oldendorf p. 61

MRI contrast: Thermal noise (Brownian motion)

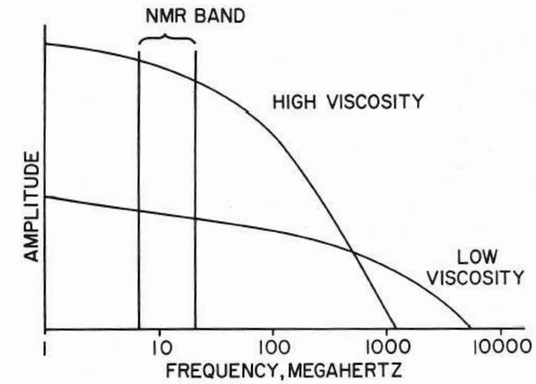


FIG. 5–5. The two curves represent the frequency distribution of the magnetic fluctuations due to thermal motion. At low viscosity (or high temperature), the thermal motion is faster; there are more high-frequency components. The area under the two curves is the same. The hydrogen resonant frequency falls somewhere in the NMR band, depending on the strength of the magnet in the scanner. At high viscosity (or lower temperature), thermal motion slows; more of the fluctuations occur in the NMR band. (Modified from Ferrar and Becker, 1971.)

Source: Oldendorf p. 54

Tissue contrast: T_1 of tissues

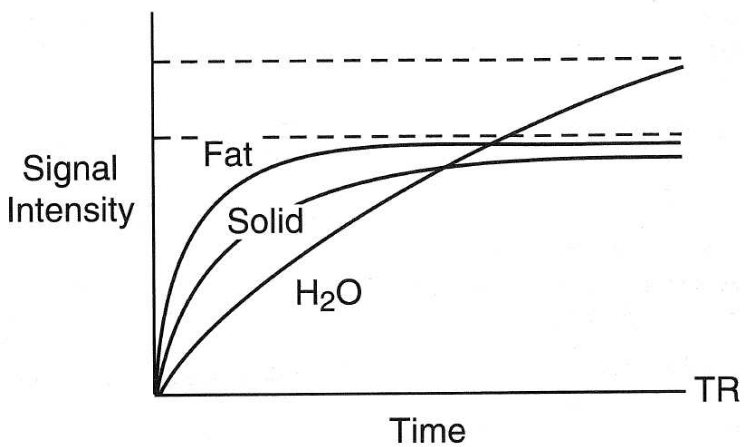


Figure 6-2. T1 recovery curves of fat, water, and a solid tissue.

Source: Hashemi p. 60

Tissue contrast: Macromolecules and microviscosity

- We have discuss T_1 and T_2 in water, but only with reference to its **bulk phase**.
- In tissues, water is bound to **hydrophilic macromolecules.**
- Polar macromolecules attract water because their chemical structure gives them a non-uniform charge distribution on their surfaces.
- Water molecules attracted in this way form a **hydration layer** around macromolecules.

Tissue contrast: Macromolecules and microviscosity

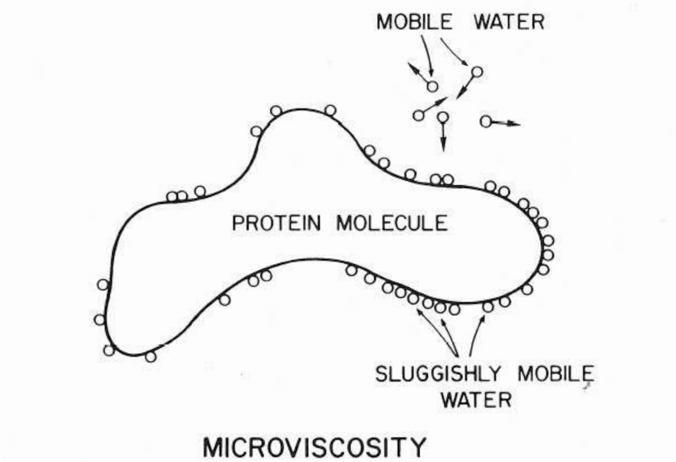


FIG. 5–6. Due to its large size, a (polar) protein molecule moves much more slowly than freely moving water molecules. Due to its polarity, it attracts the highly polar water molecules to charged sites on its surface, slowing their average motion, and shortening T_1.

Source: Oldendorf p. 55

Tissue contrast: Macromolecules and microviscosity

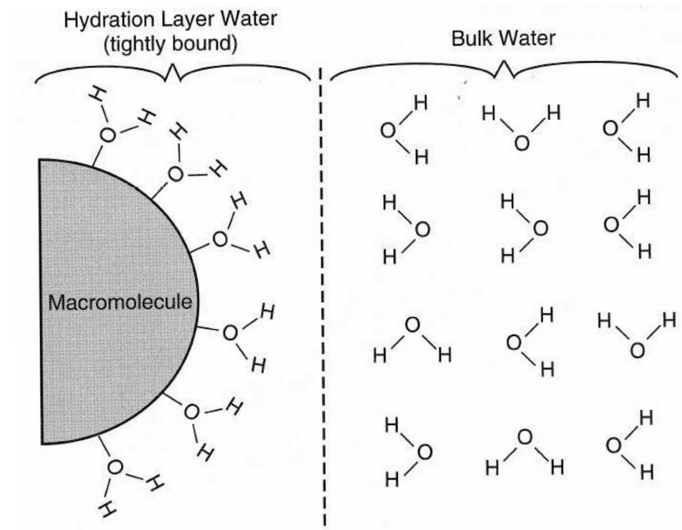


Figure 6-1. Hydration layer water.

Source: Hashemi p. 59

Tissue contrast: Macromolecules and microviscosity

- Macromolecules are much **larger and heavier** than water molecules, and so water molecules in the hydration layer have much slower thermal motion. The bandwidth of the thermal noise process will **narrow**.
- Will this affect T_1, T_2 or both, and in what way?

  ____

- Hydration layer water appears brighter in ________ -weighted images.
- If the protein content of a fluid is high enough (e.g. gels and mucinous fluids), T_2 may be shortened. These fluids appear ________________ on ________ - weighted images.

Natural tissue contrast: T_1 and T_2 in the brain

- The brain consists of gray matter, white matter and cerebrospinal fluid (CSF).
- **White matter** is myelinated. Myelin exhibits similar behavior to fat. White matter has **shorter T_1 than gray matter**.
- **Gray matter** is unmyelinated and has **an intermediate length** T_1. Its T_2 is **slightly longer than white matter**.
- **CSF** is mostly water and has the same **long T_1 long T_2**.
- Most lesions have **long T_1** since they are associated with **vasogenic edema**, which is mostly water. The T_1 of such lesions is **not as long as that of water**.

Tissue contrast: T_1 and T_2 in the brain

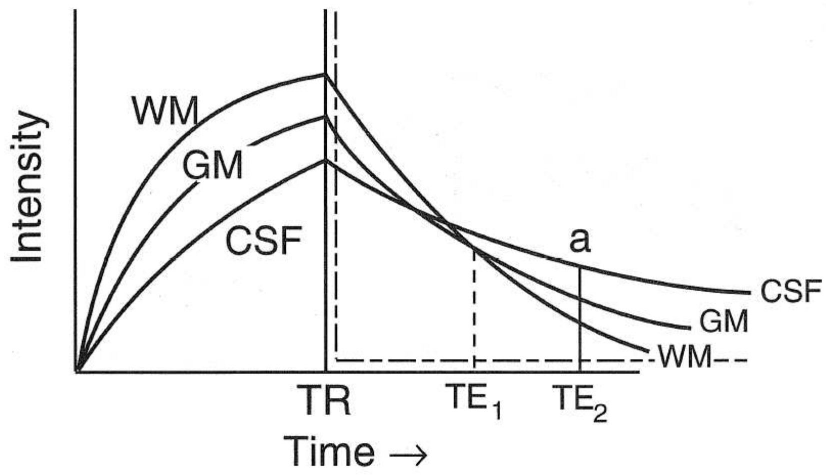


Figure 6-5. T2 decay curves of CSF, white matter, and gray matter.

Source: Hashemi p. 61

Tissue contrast: T_1 and T_2 in the brain

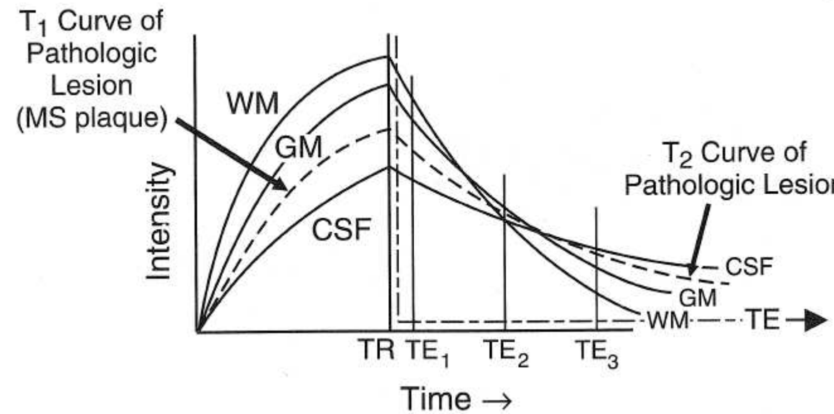


Figure 6-6. Recovery and decay curves of CSF, WM, GM, and a lesion.

Source: Hashemi p. 62

Tissue contrast: T_1 and T_2 in the brain

Table 6-1. T_1, T_2, and Proton Density of Brain Tissues*

	T_1 (msec)	T_2 (msec)	N(H)
White matter	510	67	0.61
Gray matter	760	77	0.69
Edema	900	126	0.86
CSF	2650	180	1.00

* Stark and Bradley, p. 113

Source: Hashemi p. 62

Tissue contrast: T_1 and T_2 in the brain

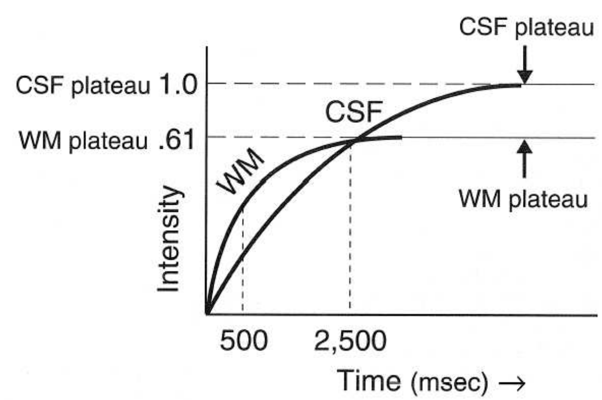


Figure 6-7. The plateau of the recovery curve of a tissue is determined by the proton density of that tissue N(H). For instance, N(CSF) is larger than N(WM).

Source: Hashemi p. 63

Tissue contrast: T_1 and T_2 in the brain

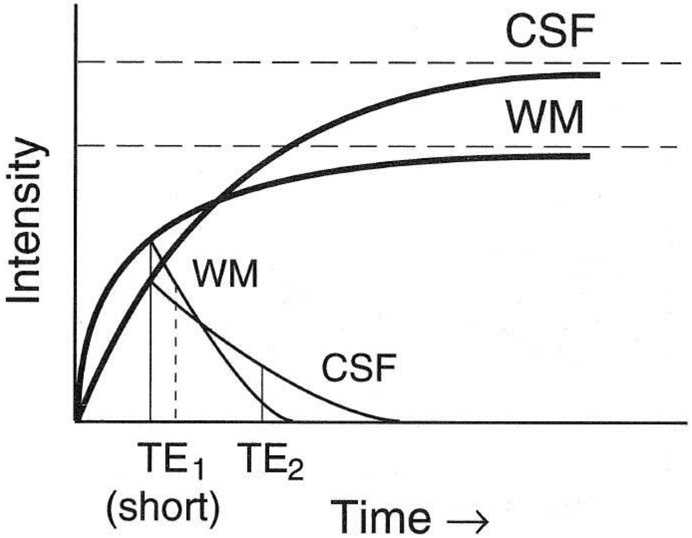


Figure 6-8. Recovery and decay curves for WM and CSF for a short TR.

Source: Hashemi p. 62

Tissue contrast: T_1 and T_2 in the brain

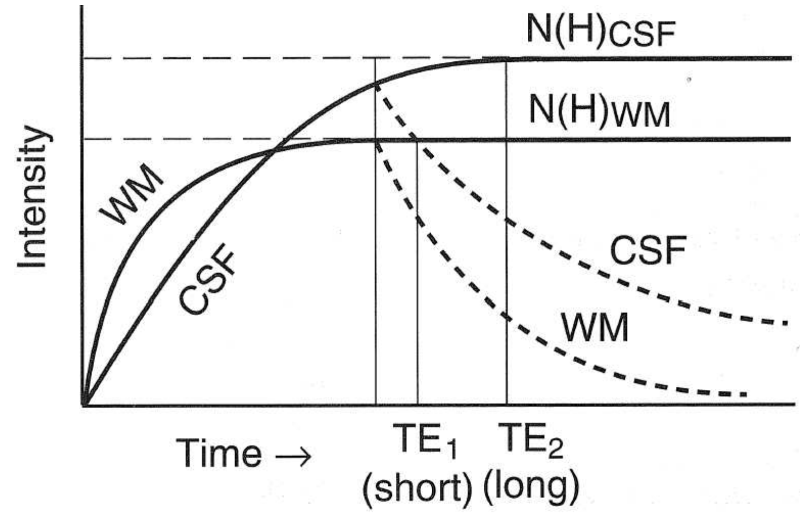


Figure 6-9. Recovery and decay curves of WM and CSF for a long TR.

Source: Hashemi p. 64

Tissue contrast in the brain to show edema

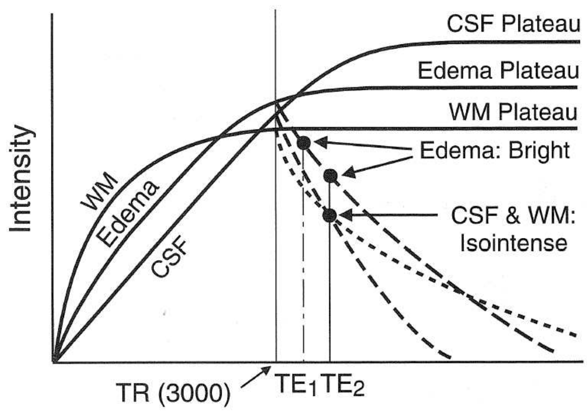


Figure 6-10. Recovery and decay curves of WM, CSF, and edema for a long TR.

Source: Hashemi p. 64

Tissue contrast in the brain

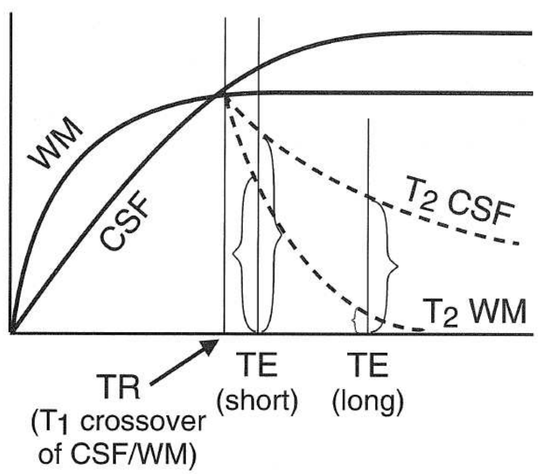
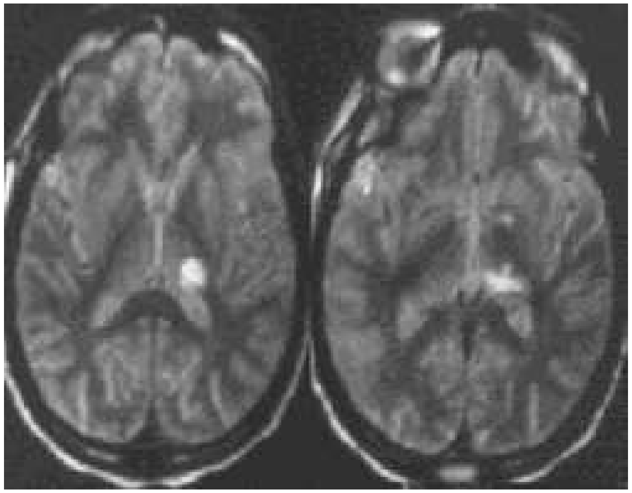


Figure 6-11. Recovery and decay curves of WM and CSF for a TR corresponding to the crossover point of CSF and WM.

Source: Hashemi p. 65

Tissue contrast: T_1 and T_2 in the brain



Brain of AIDS patient with lesion due to toxoplasmosis, a parasitic infection often acquired from cat feces. What type of weighting was used to acquire this image? ____________

Source: BrighamRad, Harvard

Contrast based on paramagnetism

- Electrons, like protons, have spin and so create a spin-induced magnetic field.
- Electrons also orbit the nucleus, creating a second magnetic field.
- In the noble gases and **most compounds in living tissues**, all electrons are paired and these fields cancel. Such materials are termed **diamagnetic**.
- In other atoms, a net field results that is ≈ 1000 times greater than the nuclear magnetic field. Such atoms are termed **paramagnetic**.
- The electron magnetic field is such a large source of noise that we can only perform NMR with nuclei that are highly resonant at specific frequencies (such as ${}^1_1$H).
- Paramagnetic fields **add considerable power** to the random local magnetic field fluctuations. Both T_1 and particularly, T_2 are reduced. The presence of a paramagnetic substance at a concentration of **only 1 ppm** can be detected.

MRI contrast: paramagnetism

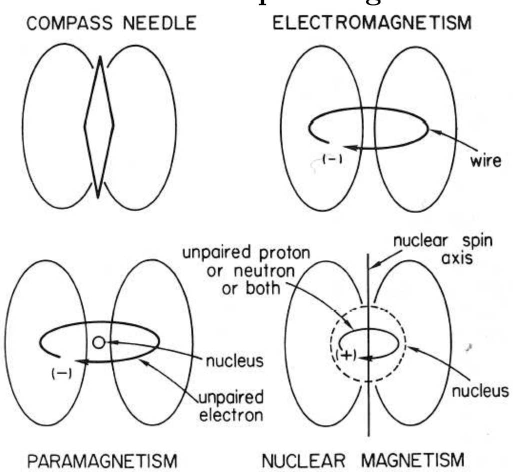


FIG. 5–7. In Chapter 3 we learned that an atomic nucleus is magnetic if it possesses a net spin from unpaired protons or neutrons (see Figures 3–1 and 3–2). Electrons orbiting the nucleus may also produce magnetism due to their orbital motion and spin. This paramagnetism is much stronger than nuclear magnetism.

Source: Oldendorf p. 57

Contrast based on paramagnetism

- Natural paramagnetism is responsible for:
  1. The contrast between active and inactive areas of the brain in **functional MRI (fMRI)**. Blood oxygen level dependent (BOLD) contrast occurs because **oxyhemoglobin is diamagnetic and deoxyhemoglobin is paramagnetic**.
  2. The dark appearance of the red nucleus, substantia nigra, globus and caudate nuclei of the brain in ________-weighted images. The nerve cells in these regions contain approximately four times the concentration of iron as other nerve cells.
- Paramagnetic materials can be **injected as tracers**. However, far larger quantities are required relative to radiotracers used in SPECT and PET. Toxicity is an issue.
- Chelated gadolinium and inhaled oxygen are non-toxic paramagnetic tracers. Nevertheless, tracers are almost never employed in MRI.
- Chelated gadolinium tracers have made **gene expression imaging** using MRI possible.

Contrast based on paramagnetism: imaging gene expression

Procedure:

- A special molecule is designed that wraps-up a highly paramagnetic gadolinium atom in an organic compound. This is called **chelation**.
- Chelation normally serves to **lower the toxicity** of the Gd. In this application, it also magnetically screens the Gd from protons in its vicinity.
- This particular chelate has a "cap" made out of **galactopyronose**.
- When a cell expresses a gene that codes for the chemical β**-galactosidase**, this enzyme is produced.
- When β-galactosidase encounters the chelate, it reacts with the cap, effectively "chewing it off".

Contrast based on paramagnetism: imaging gene expression

- The Gd atom is now no longer screened from the molecular environment and consequently reduces T_1 and T_2 in its vicinity.
- The β-galactosidase can be attached to another gene the expression of which we wish to monitor.
- When that gene is expressed, the natural enzyme and β-galactosidase will be manufactured by the cell.
- The β-galactosidase gene is termed a **reporter gene**.
- How could this procedure be used to monitor gene therapy in Parkinson's disease as discussed in Lecture 13?

____

____

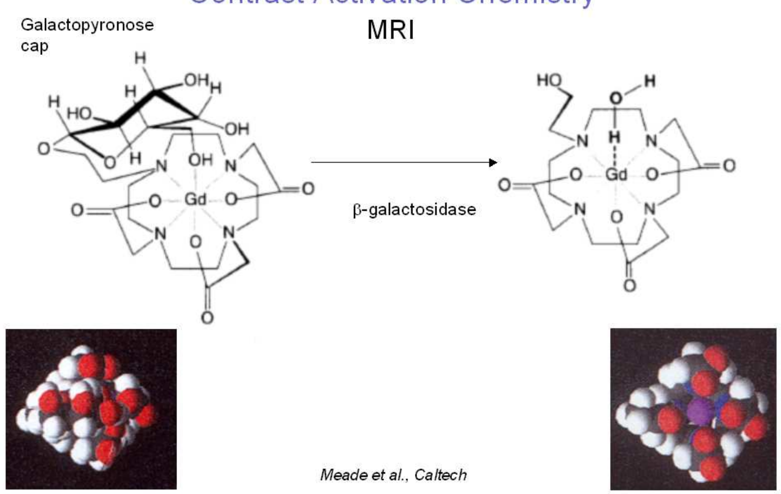
- What advantages might PET have?

____

Contrast agents in MRI: imaging gene expression

Contrast Activation Chemistry

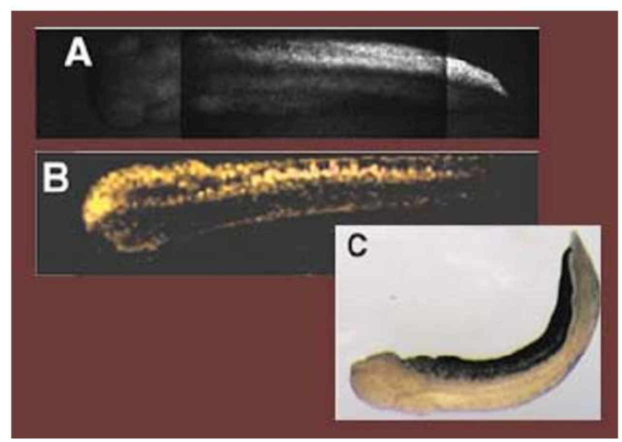
MRI



Source: Thomas Meade, Caltech

Contrast agents in MRI: imaging gene expression

Imaging Gene Expression in African Clawed Frog Embryo



Source: Thomas Meade, Caltech